

09/919,349
PD: 8/1/2000

L180 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:466702 CAPLUS

DOCUMENT NUMBER: 137:41737

TITLE: Combinations of sesquiterpene lactones and diterpene
triepoxide lactones for synergistic inhibition of
cyclooxygenase-2

INVENTOR(S): Babish, John G.; Howell, Terrence; Pacioretty, Linda

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 18 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2002077299	A1	20020620	US 2001-919349	20010731 <--
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US 2002076452	A1	20020620	US 2001-919506	20010731 <--
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PRIORITY APPLN. INFO.: US 2000-222167P P 20000801

AB A novel formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component an effective amt. of diterpene triepoxide lactone species and an effective amt. of a second component of sesquiterpene lactone species or derivs. thereof, and provides synergistic anti-inflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol. For example, a lotion designed to contain 0.1 % triptolide and 0.1% parthenolide was applied to affected areas of patients with acne rosacea and results showed improvement as compared with the placebo control.

L180 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:107101 CAPLUS

DOCUMENT NUMBER: 136:161354

TITLE: Terpene compound compositions exhibiting synergistic
inhibition of the expression and/or activity of
cyclooxygenase-2, and use as antiinflammatory agents

INVENTOR(S): Babish, John G.; Howell, Terrence M.; Pacioretty,
Linda M.

PATENT ASSIGNEE(S): Ashni Naturaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009698	A1	20020207	WO 2001-US24053	20010801 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002077350	A1	20020620	US 2001-919510	20010731 <--
PRIORITY APPLN. INFO.: US 2000-222190P P 20000801				
US 2001-919510 A 20010731				

AB A formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component, a diterpene triepoxide lactone species or a sesquiterpene lactone species and, as a second component, at least one member selected from the group consisting of a diterpene triepoxide lactone species, a sesquiterpene lactone species, a diterpene lactone species, and a triterpene species or derivs. thereof, with the proviso that the same first component cannot also serve as the second component, and provides synergistic antiinflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L180 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:10197 CAPLUS

DOCUMENT NUMBER: 130:178519

TITLE: Validation and Subsequent Development of the Derek
Skin Sensitization Rulebase by Analysis of the BgVV
List of Contact Allergens

AUTHOR(S): Barratt, M. D.; Langowski, J. J.

CORPORATE SOURCE: SEAC Toxicology Unit, Unilever Research Colworth,
Sharnbrook Bedford, MK44 1LQ, UK

SOURCE: Journal of Chemical Information and Computer Sciences
(1999), 39(2), 294-298
CODEN: JCISD8; ISSN: 0095-2338

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The DEREK knowledge-based computer system contains a subset of approx. 50 rules describing chem. substructures (toxophores) responsible for skin sensitization. This rulebase, based originally on Unilever historical inhouse guinea pig maximization test data, has been subject to extensive validation and is undergoing refinement as the next stage of its development. As part of an ongoing program of validation and testing, the predictive ability of the sensitization rule set has been assessed by processing the structures of the 84 chem. substances in the list of contact allergens issued by the BgVV (German Federal Institute for Health Protection of Consumers). This list of chems. is important because the biol. data for each of the chems. have been carefully scrutinized and peer reviewed, a key consideration in an area of toxicol. in which much unreliable and potentially misleading data have been published. The existing DEREK rulebase for skin sensitization identified toxophores for skin sensitization in the structures of 71 out of the 84 chems. (85%). The exercise highlighted areas of chem. where further development of the rulebase was required, either by extension of the scope of existing rules or by generation of new rules where a sound mechanistic rationale for the biol. activity could be established. Chems. likely to be acting as photoallergens were identified, and new rules for photoallergenicity have subsequently been written. At the end of the exercise, the refined rulebase was able to identify toxophores for skin sensitization for 82 of the 84 chems. in the BgVV list.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES
AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L180 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1976:505260 CAPLUS

DOCUMENT NUMBER: 85 105260

TITLE: Plant growth inhibitors of plant origin

AUTHOR(S): Schreiber, K.

CORPORATE SOURCE: Inst. Plant Biochem., Ger. Acad. Sci., Halle/Saale,
Ger. Dem. Rep.

SOURCE: Environmental Quality and Safety, Supplement (1975), 3(Pesticides), 483-5

CODEN: EQSSDX; ISSN: 0340-4714

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Of the 524 compds. of plant origin tested in the wheat seedling test, 71 (14%) were highly active and 126 significantly active as growth retardants. Of the active compds., 58 (11%) were also active in the pea bioassay. Only 5 of the tested compds. were shown to be antagonists of gibberellin formation in *Fusarium moniliforme*. Twelve of the 28 naturally occurring lactones (mostly sesquiterpenoid gamma.-lactones), 21 of 32

lichen constituents, and a relatively large no. of the steroids tested (28 of 90) were active.

L180 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1971:142092 CAPLUS

DOCUMENT NUMBER: 74:142092

TITLE: Correlation of structure and fragmentation modes of costunolide and its derivatives

AUTHOR(S): Sathe, R. N.; Deshpande, Mrs. N. R.; Kulkarni, G. H.; Kelkar, Govind R.; Das, K. Ganesh

CORPORATE SOURCE: Natl. Chem. Lab., Poona, India

SOURCE: Organic Mass Spectrometry (1971), 5(2), 197-202

CODEN: ORMSBG; ISSN: 0030-493X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mass spectral studies of costunolide and its lactone derivs., revealed general fragmentation modes involving the losses of 44, 55, 57, 59, 71, 73, and 83 mass units from the mol. ion. The genesis of these ions was established by high resolution, metastable transitions, and D labeling studies. Comparisons were made with the mass spectra of the C6-desoxy esters.

L180 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1963:482375 CAPLUS

DOCUMENT NUMBER: 59:82375

ORIGINAL REFERENCE NO.: 59:15314h, 15315a-h

TITLE: Mexicanin. I. A new sesquiterpene lactone related to tenulin

AUTHOR(S): Dominguez, E.; Romo, J.

CORPORATE SOURCE: Univ. Nacl. Autonoma Mexico, Mexico City

SOURCE: Tetrahedron (1963), 19(9), 1415-21

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB cf. CA 55, 22365f. The mother liquors from isolation of helenalin from *Helenium mexicanum* evapd. and the residue crystd. from C₆H₆ gave 430 mg. product, m. 246-53.dblvert., recrystd. from CHCl₂-MeOH to yield mexicanin I (I, R = H) (II), m. 257-60.degree., [α]_D 42.5.degree. (CHCl₃). (All [α]_D were detd. at 20.degree. in CHCl₃.) II (150 mg.) in 4 ml. 1:1 Ac₂O-C₅H₅N heated 1 hr. on a steam bath and dild. with H₂O, filtered, and the ppt. crystd. from Me₂CO-Et₂O gave 130 mg. I (R = Ac) (III), m. 200-3.degree., [α]_D 26.5.degree.. II (150 mg.) in 20 ml. MeOH treated with CH₂N₂ (from 2 g. MeNHCONHNO) in Et₂O 30 min. at 20.degree. and the excess CH₂N₂ destroyed with a few drops of AcOH, the mixt. filtered off, and the residue washed with Et₂O gave 90 mg. II

dipyrzoline, m. 185.degree. (decompn.). The nuclear magnetic resonance (n.m.r.) spectrum of III supported the assigned structure. II (200 mg.) in 8 ml. AcOH kept 1 hr. at 20.degree. with 150 mg. CrO₃ in 5 ml. 1:4 H₂O-AcOH, the H₂O-dild. soln. extd. with CHCl₃, the ext. washed with H₂O, 5% Na₂CO₃, and H₂O, evapd., and the residue recrystd. repeatedly from Me₂CO-Et₂O gave dehydroisomexicanin I (IV), m. 232-5.degree., [α]_D 129.degree.. II (300 mg.) in 150 ml. EtOAc hydrogenated over 80 mg. 10% Pd-C, the filtered soln. evapd., the oily residue crystd. from Et₂O, and the product crystd. from Me₂CO-C₆H₁₄ yielded di-hydroisomexicanin I (V), m. 144-6.degree., [α]_D 150-4.degree.. The cyclo-pentanone bond was reduced but the remaining bond at C-7-C-11 resisted hydrogenation. The salient features of the spectra of II, III, IV, and V, particularly the sharp signal due to a tertiary Me group, strikingly resemble those of parthenin, tenulin, and helenalin, which possess an abnormal guaianolide nucleus. V (170 mg.) in 6 ml. AcOH treated with 150 mg. CrO₃ in 5 ml. 1:4 H₂O-AcOH, the mixt. kept 80 min. at 20.degree., dild. with H₂O and extd. with CHCl₃, the ext. washed with H₂O, dried (Na₂SO₄), and evapd., the residue crystd. from Me₂CO-C₆H₁₄, and recrystd. from Me₂CO-Et₂O gave dehydrodihydroisomexicanin I (VI), m. 173-5.degree., [α]_D 184.degree.. VI (100 mg.) in 10 ml. AcOH refluxed 3 hrs. with 800 mg. powd. Zn, the filtered soln. dild. with H₂O and extd. with CHCl₃, the ext. washed with H₂O, 5% aq. NaOH, and H₂O, the dried ext. evapd., and the oily residue triturated with Et₂O gave 60 mg. needles recrystd. from Me₂CO-Et₂O to give dehydro-deacetyldihydroisotenulin (VII), m. 168-71.degree., [α]_D 20.degree.. IV (100 mg.) similarly reduced gave 45 mg. VII, m. 147-9.degree., [α]_D 22.degree. Differences in m.p. were apparently due to solvation. II (500 mg.) in 80 ml. C₆H₆ refluxed 6 hrs. with 2 ml. C₅H₁₁N and 2 ml. PhCH₂SH, the cooled mixt. washed with dil. HCl and H₂O, the dried soln. evapd., the residual oil (760 mg.) taken up in 70 ml. alc., the soln. refluxed 8 hrs. with 7 g. freshly prepd. Raney Ni with stirring, filtered, evapd., and the oily residue crystd. from Et₂O-C₆H₁₄ and recrystd. from Me₂CO-Et₂O gave deacetyldihydroisotenulin (VIII, R = H) (IX), m. 194-6.degree., [α]_D 139.degree.. IX (60 mg.) in 2 ml. 1:1 Ac₂O-C₅H₅N heated 1 hr. on a steam bath, the soln. poured into H₂O, extd. with CHCl₃, the ext. washed with dil. HCl, H₂O, dil. aq. NaOH, and H₂O, dried, evapd., and the oily residue crystd. from Et₂O and recrystd. from Et₂O-C₆H₁₄ gave dihydroisotenulin VIII (R = Ac), m. 149-50.degree., [α]_D 101.degree., 1770 cm.⁻¹ IX (40 mg.) in AcOH oxidized with CrO₃ and the isolated product crystd. from Me₂CO-C₆H₁₄ gave VII, m. 145-7.degree.. Accordingly, II is an "abnormal" guaianolide with asym. centers at C-1, C-5, C-8, and C-10 and lactone closure at C-8. The centers at C-6 and C-7 have the same configuration as in tetulin, but II differs from helenalin at C-6 and C-8 also, though both lactones have the same structural formula. II underwent a rearrangement in alk. medium to yield products of the "neo" type. II (140 mg.) in 20 ml. MeOH refluxed 3 min. with 140 mg. KOH in 2 ml. H₂O, the

mixt kept 30 min. at 20.degree., acidified with AcOH, concd., dild. with H₂O, extd. with CHCl₃, and the H₂O-washed ext. concd., treated with Et₂O, and filtered off gave 70 mg. platelets, recrystd. from CHCl₃-MeOH to give neomexicanin I (X, R = H) (XI) m. 259-63.degree., [α]_D 10.degree.. The mother liquor from the 1st crystn. evapd., the oily residue crystd. from Me₂CO-C₆H₁₄, and the product recrystd. gave methoxydihydroneomexicanin I (XII), m. 168-70.degree., [α]_D -27.degree.. Alk. treatment of II with KOH in tert-BuOH gave only XI. Acetylation of XI gave X (R = Ac), m. 170-2.degree. (Me₂CO-Et₂O), [α]_D 3.degree.; n.m.r. spectrum showed similar signals to those reported for neohelenalin and neotenulin. III (500 mg.) in 60 ml. EtOAc hydrogenated over 60 mg. prereduced PtO₂ 4 hrs., the filtered soln. evapd., and the oily residue crystd. from Et₂O and recrystd. from Et₂O-C₆H₁₄ yielded 11-epidihydro-isotenulin, m. 109.degree., [α]_D 48.degree.. Infrared, ultraviolet, and n.m.r. spectral data for most of the compds. were given.

LI80 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1962 483404 CAPLUS

DOCUMENT NUMBER: 57:83404

ORIGINAL REFERENCE NO. 57:16665d-i,16666a-h

TITLE: Terpenoids. XXXII. Absolute configuration of junenol and levojunenol and synthesis of junenol from costunolide

AUTHOR(S): Shaligram, A. M.; Rao, A. S.; Bhattacharyya, S. C.

CORPORATE SOURCE: Nat. Chem. Lab., Poona, India

SOURCE: Tetrahedron (1962), 18, 969-77

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. CA 54, 22709d; 57, 13808e. The hydrocarbon-rich fraction (b0.5 90-102.degree.) of distd. vetiver oil chromatographed on acid-washed Al₂O₃ (grades III and II) and the tail portion crystd. from petr. ether and sublimed gave levojunenol (I), m. 65.degree., [α]_D -57.degree. (l 18, all rotations in 95% alc.). I (298 mg.) heated (N atm.) 16 hrs. at 290.degree. with 446 mg. Se and the product taken up in petr. ether-C₆H₆, the concd. filtrate filtered through 30 g. Al₂O₃ (grade I) and eluted with petr. ether gave 228 mg. endalene, characterized as picrate, m. 95-6.degree., and s-trinitrobenzene deriv., m. 112.5-13.0.degree.. I (1.024 g.) in 25 ml. AcOH hydrogenated 4 hrs. with 40 mg. prereduced PtO₂ and the product (970 mg.) sublimed gave dihydrolevojunenol (II), m. 115.degree., [α]_D +-.0.degree. (C 2.6). I (970 mg.) in 60 ml. dry EtOAc at -5.degree. ozonized 5 hrs. with evolution of HCHO and the mixt. evapd. at 40.degree. in vacuo, the ozonide decompd. by heating in 30 ml. H₂O on a steam bath 4 hrs. and the aq. layer extd. with Et₂O, washed with aq. NaHCO₃ and the neutral product isolated, the liquid residue (820 mg.) distd. at 135.degree. 0.1 mm. and the solid product sublimed gave 740 mg.

oxo alc. (III), $C_{14}H_{22}O_2$, m. 43.degree., $[\alpha]_D -11.5$.degree. (c 2.00). The properties of I and its derivs. agree with those of an optical antipode of the dextrorotatory alc., junenol. III (420 mg.) in 4 ml. $(HOCH_2CH_2)_2O$ heated (N atm.) 2 hrs. with 400 mg. KOH and 0.7 ml. 85% $N_2H_4.H_2O$ at 110-15.degree. with occasional shaking and the H_2O evapd. at 195.degree., the mixt. refluxed 4 hrs. at 190.degree. and the cooled product dild. with 30 ml. H_2O , neutralized at 0.degree. with dil. HCl and extd. with Et_2O , the ext. neutralized and the dried soln. evapd., the product (383 mg.) dehydrogenated with 530 mg. Se at 280.degree. and the product chromatographed over 30 mg. Al_2O_3 (grade I) gave 2-Me $_2$ CHC $_{10}H_7$, characterized as s-trinitrobenzene deriv., m. 107.degree. Santanolide a (11.3 g., prepd. according to Kovacs, et al., CA 50, 11285f, from L-santonin) in 100 ml. Et_2O stirred at -10.degree. 1 hr. with addn. of 435 mg. $LiAlH_4$ in 100 ml. dry Et_2O and the mixt. stirred 2 hrs. before warming to 20.degree., the mixt. decompd. with H_2O and extd. with Et_2O gave 10.2 g. amorphous material showing a pos. Fehling test. The reduced product (3.17 g.) taken up in 14 ml. distd. $(HOCH_2CH_2)_2O$ and shaken 30 min. at 20.degree. with 6 ml. 85% $N_2H_4.H_2O$, the soln. refluxed 2 hrs. (N atm.) with 3 g. KOH at 110-15.degree. and the H_2O evapd. at 195.degree., the soln. refluxed 3 hrs. at 190.degree. and the cooled product dild. with 50 ml. H_2O , repeatedly extd. with Et_2O and the residue on evapn. (700 mg.) chromatographed over 30 g. Al_2O_3 (grade III), eluted with 200 ml. 9:1 petr. ether- C_6H_6 and the fraction sublimed gave 388 mg. alc., $C_{15}H_{28}O$ (IV), m. 53-4.degree.. As expected, the infrared spectrum of IV differed from that of II, and the same series of reactions was applied to santanolide c (V). Costunolide (21.4 g., m. 106.degree.), $[\alpha]_D 128$.degree. in 200 ml. AcOH contg. 10 ml. 65% $HClO_4$ hydrogenated with prereduced PtO_2 and the filtered soln. concd. to 70 ml., neutralized with Na_2CO_3 and extd. with Et_2O gave 6.3 g. V, m. 153-4.degree. (alc.), $[\alpha]_D 54.9$.degree., also prepd. by hydrogenating a mixt. of costunolide and dehydrocostus lactone. V (9.9 g.) in 100 ml. Et_2O partially reduced with 500 mg. $LiAlH_4$ in 100 ml. Et_2O and totally reduced by Huang Minlon reduction gave material, purified by chromatography and sublimation to yield 379 mg. alc. (VI), m. 115.degree., $[\alpha]_D \pm 0$.degree. (c 1.52), giving an infrared spectrum completely superimposable on that of II, and an identical n.m.r. spectrum, showing that VI and II are either identical or enantiomorphs. Mixed m.p. of VI and II gave a 20.degree. depression and the lack of identity was confirmed by measurement of rotatory dispersion curves. The mol. rotation difference ($\Delta M = -129$.degree.) between I and II is neg. but of the same magnitude as that between junenol (VII) and VI, which is of the same sign as that between eudesmol and dihydroeudesmol. Accordingly the abs. configuration of VII, I, and II can be depicted. I is the 1st naturally occurring eudesmanic compd. contg. both α -oriented C-10 Me and C-7 Me $_2$ CH groups. The acid cyclization of dihydrocostunolide (VIII) gave a mixt. of 2 closely related lactones,

the endocyclic unsatd. lactone (IX) and the exocyclic unsatd. isomeride (X), sepd. by column chromatography. VIII (m. 77.degree., [α]_D 113.degree.) cyclized in AcOH and Ac₂O and the mixt. (62 g.) chromatographed on 2.4 kg. Al₂O₃ (grade III) and eluted successively with 10 l. petr. ether, 6 l. 1:1 petr. ether-C₆H₆, 6 l. C₆H₆, 6 l. alc., and 6 l. AcOH gave 27 g. fraction, m. 128.degree.; 0.8, 0.5, and 0.5 g. fraction, m. 60.degree.; and 24.5 g. fraction, m. 132.degree.. The 1st fraction repeatedly recrystd. from alc. and C₆H₁₄ and sublimed gave IX, m. 140.degree., [α]_D 85.degree. (c 1.402, CHCl₃), hydrogenated in AcOH with prereduced PtO₂ to give V. The last fraction recrystd. from C₅H₁₂ and sublimed gave the lactone X, m. 140.degree. [α]_D 140.degree. (c 3.5, CHCl₃), hydrogenated in AcOH with prereduced PtO₂ to give santanolide. X (1.1 g.) in 30 ml. dry EtOAc ozonized 5 hrs. at -5.degree. with evolution of HCHO, the product crystd. from alc. and sublimed at 150.degree./0.05 mm. gave 800 mg. oxo lactone (XI), m. 220.degree. [α]_D 71.48.degree. (c 1.525, CHCl₃). X (7.15 g.) in 150 ml. anhyd. Et₂O at -10.degree. stirred 1 hr. with addn. of 420 mg. LiAlH₄ in 100 ml. Et₂O and the mixt. stirred 2 hrs. at -10.degree. and 1 hr. at 20.degree., the washed and dried Et₂O layer evapd. in vacuo and the partially reduced lactone (6.8 g.) heated 5 min. on a steam bath in 40 ml. (HOCH₂CH₂)₂O and 11 ml. 85% N₂H₄.H₂O, the clear soln. kept 30 min. at 20.degree. and refluxed 2 hrs. at 110-15.degree. with 6 g. KOH, treated at 60.degree. with 20 ml. dry C₆H₆ and the C₆H₆ carefully evapd. at 130.degree. the procedure repeated 3 times and the H₂O-free soln. refluxed 2 hrs. at 150.degree., the cooled mass dild. with 50 ml. H₂O and extd. with Et₂O, the product (800 mg.) chromatographed on 30 g. Al₂O₃ (grade III) and the column eluted with 200 ml. 9:1 petr. ether-C₆H₆, the fraction crystd. from petr. ether and sublimed gave VII, m. 61-2.degree., [α]_D 51.degree. (C 2.45). Ultraviolet, infrared, and nuclear magnetic resonance spectra were given.

L180 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1962:423334 CAPLUS

DOCUMENT NUMBER: 57:23334

ORIGINAL REFERENCE NO : 57:4699b-g

TITLE: Conversion of costunolide to junenol

AUTHOR(S): Shaligram, A. M.; Rao, A. S.; Bhattacharyya, S. C.

CORPORATE SOURCE: Natl. Chem. Labs., Poona, India

SOURCE: Chem. Ind. (London) (1961) 671

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB (All [α]_D in EtOH.) Previously (CA 54, 22709d) the abs. configuration was established of the enantiomeric sesquiterpene alcs. junenol (I) and levojunenol (II), on the basis of conversion of santanolide c (III) to dihydrojunenol (IV). The structure and conversion

of the lactone V to dextrorotatory I was now described. Cyclization of VI gave a product (VIa), m. 117.degree., much lower than that of the lactone (VII), previously (CA 54, 3489d) obtained by cyclization of VI. Chromatography of VIa gave VII, m. 140.degree., [α]_D 85.degree. (c 1.402), giving III on catalytic hydrogenation, giving no CH₂O on ozonolysis, this structure also being in agreement with its infrared (ν 790 and 1794 cm.⁻¹) and ultraviolet spectra (ϵ 210 287, ϵ 215 1435, ϵ 220 385), and an isomer (V), m. 140.degree., [α]_D 140.degree. (c 3.55), this structure being assigned on the basis of infrared (ν 885, 1633, and 1764 cm.⁻¹) and ultraviolet spectra (ϵ 210 377, ϵ 215 120, ϵ 220 75), giving santanolide A on catalytic hydrogenation, giving on ozonolysis CH₂O (dimedon deriv. m. 189.degree.) and the oxo lactone (VIII), m. 210.degree., [α]_D 71.degree. (c 1.525). V was converted to d-I as described previously for the conversion of III to IV. d-I m. 61-2.degree., [α]_D 51.degree. (c 2.45), its infrared spectrum being identical with that of II.

L180 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1962:38646 CAPLUS

DOCUMENT NUMBER: 56:38646

ORIGINAL REFERENCE NO.: 56:7368c-i

TITLE: CXXXI. Isolation and structure of costunolide, balchanolide, isobalchanolide, and hydroxybalchanolide, sesquiterpenic lactones of germacrane type from *Artemisia balchanorum*

AUTHOR(S): Krasch, H.; Herout, V.; Suchy, M.; Sorm, F.

CORPORATE SOURCE: Ceskoslov. Akad. Ved., Prague

SOURCE: Collection Czechoslov. Chem. Commun. (1961), 26, 2612-23

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB Costunolide (I), m. 106.degree. (MeOH), [α]_D 128.degree. (c 10.5, CHCl₃), isobalchanolide (II), m. 133.degree. (iso-Pr₂O-Me₂CO), [α]_D 122.degree. (c 2.08, CHCl₃), balchanolide (III), m. 154.degree. (iso-Pr₂O-Me₂CO), [α]_D 183.degree. (c 1.84, CHCl₃), and hydroxybalchanolide (IV), m. 163.degree. [α]_D 105.degree. (c 2.71, EtOH). Hydrogenation of I in MeOH over 5% Pd on C gave dihydrocostunolide (V), m. 79-80.degree. (MeOH). Hydrogenation of I in AcOH over PtO₂ gave oily hexahydrocostunolide. If 2 drops of 70% HClO₄ were added to the mixt., the H uptake amounted to 2.0 double bonds and santanolide C (VI) was the chief product, m. 155.degree. (EtOH), [α]_D 50.1.degree. (c 4.0, CHCl₃), along with 2 compds., m. 114.degree. (MeOH) and m. 79.degree., isolated by chromatography. Refluxing V with AcOH and Ac₂O, evapg. the mixt., and crystg. from MeOH

gave a compd., m. 122.degree., whose recrystn. from 1:5 C6H6-petr. ether gave 3-santenolide (VII), m. 135.5.degree.. Hydrogenation of VII in AcOH over PtO2 (H uptake amounted to 1.05 double bonds) followed by crystn. and chromatography gave VI along with santanolide A, m. 153.degree. (80% aq. EtOH). The location of the double bonds in I (CA 54, 3489b) was verified by ozonization of V in AcOH and decompn. of the ozonides in boiling HNO3: the chief product, a lactonedicarboxylic acid, Rf 0.38 (BuOAc-2% HCO2H), was identical with that prepd. earlier from artabsin.

Acetylisobalchanolide, m. 139-40.degree., [α]_D 18.5.degree. (c 1.8, CHCl3), was hydrogenated in MeOH over PrO2 to give tetrahydroacetylisobalchanolide (VHI), m. 125.degree. (iso-Pr2O), identical with tetrahydroacetylbalchanolide, prepd. earlier. Hydrolysis of VIII with K2CO3 in MeOH followed by oxidn. of the oily product with CrO3 in AcOH gave an oxo lactone, C15H24O3, m. 136.5.degree. (iso-Pr2O), identical with that prepd. earlier from arctiopicrin and cnicin. Oxidn. of II-IV with satd. aq. KMnO4 gave a mixt. of (CH2CO2H)2 and MeCOCH2CH2CO2H, identified by paper chromatography. Oxidn. of III with CrO3 in C5H5N gave an oxo lactone, C15H20O3, m. 110.degree. (iso-PrO2). Hydrogenation of IV in AcOH over PtO2 gave tetrahydrohydroxybalchanolide C15H26O4, m. 101.degree. (iso-Pr2O-Me2CO), whose oxidn. with CrO3 in AcOH gave a hydroxy oxo lactone, C15H24O4 (IX), m. 127.degree. (isoPr2O-Me2CO). Structures of II-IV and some of their derivs. were suggested. II and III differ in the location of the double bonds, or, in their steric arrangement (cis-trans-isomerism) only.

L180 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1961:137670 CAPLUS

DOCUMENT NUMBER: 55:137670

ORIGINAL REFERENCE NO.: 55:26013g-i,26014a-i,26015a-i,26016a-d

TITLE: Cedrol: stereochemistry and total synthesis

AUTHOR(S) Stork, Gilbert; Clarke, Frank H., Jr.

CORPORATE SOURCE: Columbia Univ.

SOURCE: J. Am. Chem. Soc. (1961), 83, 3114-25

CODEN: JACSAT, ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB The total stereospecific synthesis of natural cedrol (I) was described.

Me2C(CN)CH(CN)CO2Et (II), b0.01 about 99-114 degree., b4 120-7.degree. (with decompn.), (250 g.) in 232 g. Me3COH treated with 87 g. CH2:CHCN and 50 cc. 40% choline in MeOH, the mixt. kept 6 hrs. at 0.degree., 18 hrs. at room temp., and 40 hrs. at 50 degree., cooled until crystals of Me3COH appeared, the top layer evapd. on the steam bath in vacuo, the combined residue and bottom layer dild. with Et2O, washed, evapd., the combined residues (638 g.) from 2 runs dissolved in 1300 cc. concd. HCl and 1300 cc. H2O, the soln. refluxed 48 hrs., evapd. on the steam bath, cooled,

filtered, evapd. to dryness, the residue treated with abs. EtOH, filtered, the filtrate (3500 cc.) refluxed 4.5 days with stirring with 700 cc. concd. H₂SO₄, 1 l. of EtOH distd., the residual soln. cooled, poured into satd. aq. NaCl, the oily layer worked up with Et₂O, and distd. gave 480 g. Me₂C(CO₂Et)CH(CO₂Et)(CH₂)₂CO₂Et (III), b_{0.01} about 154-6.degree., and 158 g. residue, which hydrolyzed and reesterified gave more III. III refluxed 3 hrs. in C₆H₆ with powd. Na yielded 64% di-Et 3,3-dimethylcyclopentan-2-one-1,4-dicarboxylate (IV), b_{132-3.degree.} (in vacuo). PhCH₂OH (34.0 g.), 48 g. MeCHBrCO₂H, and about 0.5 g. p-MeC₆H₄SO₃H in 150 cc. C₆H₆ refluxed 18 hrs. with azeotropic removal of H₂O gave 55.5 g. MeCHBrCO₂CH₂Ph (V), b₇ 139-41.degree. IV (50.0 g.) in 80 cc. dry C₆H₆ and 6.0 g. NaH in 100 cc. dry C₆H₆ refluxed until the H evolution ceased, decanted, the soln. distd. to remove 155 cc. C₆H₆, treated with the Na salt of 47.5 g. V in 100 cc. dry HCONMe₂, the mixt. heated at 50.degree. under N, kept 1 week, combined with the soln. of a 2nd run from 71.1 g. IV, and worked up yielded 179 g. 1-PhCH₂ ester (VI) of the HO₂CCHMe deriv. (VII) of IV, b_{175-92.degree.} (in vacuo). VI (77.0 g.) in 150 cc. EtOAc hydrogenolyzed during 35 min. over 8.0 g. 10% Pd-C at an initial pressure of 50.0 lb. yielded 47.0 g. VII, prisms, m_{113-15.degree.} (cyclohexane). Na salt (11.6 g.) of VII in 100 cc. dry C₆H₆ contg. 1.0 cc. C₅H₅N with 15 cc. (COCl)₂ added slowly to excess CH₂N₂ in Et₂O from 45 g. H₂NCON(NO)Me, the mixt. kept 1 hr. at 0.degree., evapd. on the steam bath, and the residual crude diazoketone treated in 150 cc. dry Et₂O with cooling with dry HCl gave 10.7 g. 1-ClCH₂COCHMe deriv. (VIII) of V, m_{72-3.degree.} (cyclohexane). VIII (19.2 g.) and 20 g. powd. KI in 250 cc. AcOH treated slowly with stirring at 25.degree. with 100 g. Zn dust, stirred 6 hrs., dild. with 50 cc. H₂O, stirred overnight, filtered, the filtrate evapd., the residue partitioned between H₂O and Et₂O, and the Et₂O soln. worked up gave 17.1 g. 1-AcMeCH deriv. (IX) of V, m_{55-60.degree.} (petr. ether); semicarbazone m_{191-3.degree.} (aq. EtOH). Crude IX (4.3 g.) in 30 cc. dry Me₃COH and 0.7 g. K in 70 cc. dry Me₃COH refluxed 3 hrs. under N, dild. with H₂O, and extd. with Et₂O gave 1.47 g. mobile oil; a 0.4-g. portion, 0.45 g. semicarbazide, 1.65 cc. C₅H₅N, and 8 cc. EtOH refluxed 1.5 hrs. and kept overnight yielded the semicarbazone of X, m_{174-6.degree.} (EtOAc-cyclohexane). IX (20.1 g.) and 3.0 g. K in 300 cc. dry Me₃COH kept 10 min. at room temp. gave 18.6 g. crude aldol, which, refluxed 1 hr. with 2.0 g. p-MeC₆H₄SO₃H.H₂O in 400 cc. C₆H₆, yielded 15.2 g. XI, m_{46-56.degree.} (petr. ether); 23.6 g. crude XI recrystd. twice from petr. ether gave 10.8 g. of 1 isomer, m_{65-7.degree.}, of XI. XI (504 mg.), m_{65-7.degree.}, in 16 cc. abs. EtOH hydrogenated 20 min. at 25.4.degree. over 136 mg. 10% Pd-C yielded 325 mg. XII, m_{33.5-35.0.degree.} (petr. ether); 2,4-dinitrophenylhydrazone (XIII) m_{160-1.degree.}; recrystd. from EtOAc-EtOH, it gave needles, which slowly changed to prisms on standing in the soln. XI (307 mg.) in 2 cc. dry tetrahydrofuran and 15 cc. dry liquid NH₃ treated with stirring with 15-20 mg. Li and then with 0.6 g. NH₄Cl, the NH₃ evapd., and the residual

yellowish oily XII (271 mg.) chromatographed from petr. ether on Al_2O_3 yielded oily colorless XII; XIII m. 152-4.degree (EtOAc-EtOH). XII (655 mg.) in 10 cc 80% EtOH refluxed 36 hrs. under N with 2.0 g. KOH, poured into H_2O , washed with Et_2O , acidified with concd. HCl, extd. with Et_2O , the gummy residue (528 mg.) from the ext. refluxed 3 hrs. with 6 cc. Ac_2O , evapd. under a stream of N, and the dark residue sublimed in vacuo at 160-70.degree gave 174 mg. anhydride (XIV), prisms, m. 171-3.degree. (Et_2O). The XIV refluxed 20 hrs. with 6 cc. 50% aq. dioxane and the oily product treated with MeCHN_2 from 5 cc. $\text{EtO}_2\text{CN}(\text{NO})\text{Et}$ yielded 102 mg. XII; XIII m. 159-61.degree XII (1.03 g) in 10 cc CHCl_3 and 10 cc. $(\text{CH}_2\text{SH})_2$ satd. with dry HCl and kept at 0.degree. overnight yielded 0.86 g. XV, m. 75-6.degree. (pentane). XV (1.32 g) in 125 cc. abs. EtOH stirred 15 hrs. at reflux with 50 g. Raney Ni alloy gave 0.86 g. di-Et ester (XVI) of dl-norcedrenedicarboxylic acid (XVII), mobile oil. XVII (0.82 g.) and 2.0 g. KOH in 10 cc. 95% EtOH refluxed 24 hrs., poured into H_2O , and acidified with 10 cc. concd. HCl gave 0.62 g. XVII, m. 221-3.degree. (Et_2O -pentane). XVII (300 mg.) in Me_2CO with 410 mg. quinine in acetone yielded 252 mg. quinine salt (XVIII) of (-)-XVII, m. 209-10.degree. ($\text{CHCl}_3\text{Me}_2\text{CO}$), $[\alpha]_D^{25} -122$.degree. (c 1.00, CHCl_3). XVII (121 mg.) shaken 15 min. with 5 cc. 6N HCl gave 46 mg. (-)-XVII, m. 212-13.degree., $[\alpha]_D^{25} -38.9 \pm 1.5$.degree. (c 1.08, Me_2CO), natural (-)-XVII m. 213-14.degree., $[\alpha]_D^{25} -38.3 \pm 1.0$.degree. (c 1.09, Me_2CO) (-)-XVII (10.00 g.) with excess CH_2N_2 in Et_2O yielded 10.59 g. XIX (R = CO_2H) (XX), b.p. 95-132.degree.. XX (10.5 g.) and 2.4 g. KOH in 35 cc. abs. EtOH refluxed 2 hrs. gave about 2 g. unchanged XX and 6.20 g. XIX (R = CO_2Me) (XXI), m. 129-32.degree.. XXI (8.05 g.) and 20 cc. $(\text{COCl})_2$ kept 1.5 hrs. at room temp., dild., evapd. with C_6H_6 , the residual XIX (R = COCl) treated 1 hr. with CH_2N_2 from 45 g. $\text{H}_2\text{NCON}(\text{NO})\text{Me}$ in Et_2O , the resulting crude XIX (R = CON_2) in 50 cc. dry Et_2O satd. with dry HCl, evapd. in vacuo on the steam bath, the XIX (R = COCH_2Cl) treated with cooling and stirring with 9 g. KI in 100 cc. 80% AcOH and 45 g. powd. Zn, and the mixt. stirred at room temp. overnight yielded 7.73 g. crude XIX (R = Ac) (XXII), 2,4-dinitrophenylhydrazone m. 140-2.degree. (cyclohexane). XXII (7.73 g.) and 3.0 g. KOH in 120 cc. dry Me_3COH refluxed 3 hrs. yielded 4.90 g. XXIII, m. 202-4.degree. (dioxane). XXIII (2.00 g.) refluxed 17 hrs. with stirring with 2.00 g. LiAlH_4 in 50 cc. dry Et_2O gave 1.91 g. (crude) XXIV, m. 120-1.degree. (cyclohexane). Crude XXIV oxidized with $\text{CrO}_3\text{-C}_5\text{H}_5\text{N}$ and the crude product chromatographed on Al_2O_3 yielded XXV; 2,4-dinitrophenylhydrazone m. 146-7.degree.. XXIII (2.84 g.) in 50 cc. abs. EtOH contg. 0.10 g. p- $\text{MeC}_6\text{H}_4\text{SO}_3\text{H}$ H_2O distd. during 4 hrs. to remove 53 cc. distillate gave 2.82 g. oily mixt. of the enol ethers; the crude mixt. in 25 cc. dry Et_2O reduced with 1.0 g. LiAlH_4 in 150 cc. Et_2O and the crude product (2.45 g.) refluxed 1.5 hrs. with 0.20 g. p- $\text{MeC}_6\text{H}_4\text{SO}_3\text{H} \cdot \text{H}_2\text{O}$ in 50 cc. C_6H_6 yielded 508 mg. XXIV. XXIII (5.21 g.) in dry Et_2O reduced with 7.77 g. LiAlH_4 in 250 cc. dry Et_2O , the crude foamy product (4.11 g.) treated 17 hrs. at room temp. with 8.43 g. CrO_3 in 84

cc. C₅H₅N, the mixt. poured into 750 cc. Et₂O, filtered, and the filtrate worked up gave 2.81 g. pale yellow oily aldehyde-ketone; a 2.50-g. portion refluxed 1.45 hrs. with 12.5 g. KOH in 500 cc. H₂O at about 50.degree. and 90 mm., extd. with Et₂O, and the crude oily product (2.02 g.) chromatographed on Al₂O₃ yielded 1.47 g. XXVI; 2,4-dinitrophenylhydrazone, brilliant red prisms, m. 164-7.degree. (MeOH). XXVI (527 mg.) in 10 cc. abs. EtOH hydrogenated 1 hr. at 23.degree. gave 524 mg. oily XXV; 2,4-dinitrophenylhydrazone, yellow needles changing to prisms on standing in soln., m. 146-7.degree. (MeOH). XXIV (219 mg.) in 2.2 cc. C₅H₅N treated 23 hrs. at room temp. with 224 mg. CrO₃ in 2.2 cc. C₅H₅N yielded 190 mg. XXV. XXV (164 mg.) reduced during 17 hrs. with 0.40 g. LiAlH₄ in 30 cc. Et₂O gave 140 mg. XXIV. XXV (446 mg.) in dry Et₂O added slowly to MeLi from 1.8 g. Li and 6 cc. MeI in 40 cc. dry Et₂O and the mixt. refluxed 18.5 hrs. with stirring gave I, collected in 4 fractions: 380 mg., m. 80-1.degree.; 340 mg., m. 83-7.degree.; 284 mg., m. 85-7.degree.; 215 mg., m. 86-7.degree., needles, [α]_D²⁵ 10.5 \pm 0.8.degree. (c 5.00); natural I m. 86-7.degree., [α]_D²⁵ 9.9 \pm 0.4.degree. (c 5.00, CHCl₃).

L180 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1950:711 CAPLUS

DOCUMENT NUMBER: 44:711

ORIGINAL REFERENCE NO.: 44-138f-i,139a-b

TITLE: Helenalin. I. Isolation and properties

AUTHOR(S): Adams, Roger; Herz, Werner

SOURCE: J. Am. Chem. Soc. (1949), 71, 2546-51

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. Clark, C.A. 30, 8236.2. Helenalin (I), C₁₅H₁₈O₄, was isolated from *Helenium microcephalum* by the method of C. in av. yields of 0.38% and, crystd. 3 times from abs. EtOH, m. 176-8.degree.; the residue, crystd. 3 times from abs. EtOH, m. 165.5-6.degree., [α]_D²⁵ -102.8.degree. (0.0728 g. in 2 ml. 95% EtOH); the infrared spectrum is identical with that of C.'s prepn. The Ac deriv. (II), m. 179.5-80.5.degree., absorption max. at 221 and 316 m. μ . (ϵ 12, 600 and 61). o-Bromobenzoyl deriv. of I, m. 162-3.degree., p-nitro-benzoyl deriv. of I, with 0.5 mol. C₆H₆, m. 111.degree.; 3,5-dinitrobenzoyl deriv., with 0.5 mol. C₆H₆, m. 213.degree.. Tetra-hydrohelenalin (III), m. 175-6.degree., infrared spectrum given; Ac deriv. (IV), m. 145.degree. (prepd. by acetylation of III or by reduction of II in AcOEt over Pt oxide); the spectra of III and IV are similar [absorption max. at 287 m. μ . (ϵ 36)]. IV (115 mg.) and 64 mg. piperonal in 2 ml. abs. EtOH, treated with 5 ml. satd. EtOH-HCl and kept 18 hrs., give the piperonylidene deriv. of II, C₂₅H₂₅O₇Cl, pale yellow, m. 214.degree.. I (50 mg.) in 1 ml. AcOH, treated with 1.03 g. Br in 15 ml.

AcOH at room temp., gives 71 mg. dibromohelenalin (V), decomp. 130.degree.; recrystn. of V from 50% EtOH or 50% AcOH gives bromohelenalin, m. 164.5.degree., absorption max. at 248 and 314 m.mu. (epsilon. 6300 and 97); reduction over Pt oxide gives III. II and Br in Ac-OH, irradiated with an elec. light, give a di-Br deriv., decomp. 153-4.degree.; boiled 0.5 hr. with 50% EtOH, it gives the Br deriv., m. 153.5.degree.. I and NH2OH.HCl in abs. EtOH contg. AcONa, refluxed 16 hrs., give the compd. C15H22N2O5, amorphous, m. 200-3.degree. (decompn.). I (1 g) and 4 g. (iso-PrO)3Al in 20 ml. iso-PrOH, refluxed 5 hrs., the solvent removed by slow distn., 20 ml. iso-PrOH added, the distn. continued until the test for Me2CO is neg., the product decompd. with 25 ml. 10% H2SO4, and extd. with ether, give 100 mg. of the compd., C15H20O4, b0.1 200-30.degree. (bath temp.), it did not yield a solid ester; in 1 expt. there resulted 29 mg. of a compd., m. 196-201.degree., which may be an intramol. oxidation-reduction product. I and O3 give 50-60% HCHO; II gives 45% HCHO. Chem. and phys. evidence establishes the presence of the grouping RCOCH:CR2, possibly a part of a 5-membered ring, and makes likely the presence of a lactone ring. These functional groups account satisfactorily for all 4 O atoms and for 1 of the double bonds. The other double bond is unconjugated and part of a terminal CH2 group.

L189 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002.107101 CAPLUS

DOCUMENT NUMBER: 136:161354

TITLE: Terpene compound compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2, and use as antiinflammatory agents

INVENTOR(S): Babish, John G.; Howell, Terrence M.; Pacioretty, Linda M.

PATENT ASSIGNEE(S): Ashni Naturaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002009698	A1	20020207	WO 2001-US24053	20010801
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W AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 US 2002077350 A1 20020620 US 2001-919510 20010731
 PRIORITY APPLN. INFO. US 2000-222190P P 20000801
 US 2001-919510 A 20010731
 AB A formulation is provided that serves to inhibit the inflammatory response
 in animals. The formulation comprises, as a first component, a diterpene
 triepoxide lactone species or a sesquiterpene lactone species and, as a
 second component, at least one member selected from the group consisting
 of a diterpene triepoxide lactone species, a sesquiterpene lactone
 species, a diterpene lactone species, and a triterpene species or derivs.
 thereof, with the proviso that the same first component cannot also serve
 as the second component, and provides synergistic antiinflammatory effects
 in response to phys. or chem. injury or abnormal immune stimulation due to
 a biol. agent or unknown etiol.
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L189 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:466702 CAPLUS
 DOCUMENT NUMBER: 137:41737
 TITLE: Combinations of sesquiterpene lactones and diterpene
 triepoxide lactones for synergistic inhibition of
 cyclooxygenase-2
 INVENTOR(S): Babish, John G.; Howell, Terrence; Pacioretty, Linda
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 18 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002077299	A1	20020620	US 2001-919349	20010731
US 2002076452	A1	20020620	US 2001-919506	20010731
PRIORITY APPLN. INFO.		US 2000-222167P P 20000801		
AB A novel formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component an effective amt. of diterpene triepoxide lactone species and an effective amt. of a second component of sesquiterpene lactone species or derivs.				

thereof, and provides synergistic anti-inflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol. For example, a lotion designed to contain 0.1 % triptolide and 0.1% parthenolide was applied to affected areas of patients with acne rosacea and results showed improvement as compared with the placebo control.

L189 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:10197 CAPLUS

DOCUMENT NUMBER: 130:178519

TITLE Validation and Subsequent Development of the Derek
Skin Sensitization Rulebase by Analysis of the BgVV
List of Contact Allergens

AUTHOR(S): Barratt, M. D.; Langowski, J. J.

CORPORATE SOURCE: SEAC Toxicology Unit, Unilever Research Colworth,
Sharnbrook Bedford, MK44 1LQ, UK

SOURCE: Journal of Chemical Information and Computer Sciences
(1999), 39(2), 294-298

CODEN: JCISD8; ISSN: 0095-2338

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The DEREK knowledge-based computer system contains a subset of approx. 50 rules describing chem. substructures (toxophores) responsible for skin sensitization. This rulebase, based originally on Unilever historical inhouse guinea pig maximization test data, has been subject to extensive validation and is undergoing refinement as the next stage of its development. As part of an ongoing program of validation and testing, the predictive ability of the sensitization rule set has been assessed by processing the structures of the 84 chem. substances in the list of contact allergens issued by the BgVV (German Federal Institute for Health Protection of Consumers). This list of chems. is important because the biol. data for each of the chems. have been carefully scrutinized and peer reviewed, a key consideration in an area of toxicol. in which much unreliable and potentially misleading data have been published. The existing DEREK rulebase for skin sensitization identified toxophores for skin sensitization in the structures of 71 out of the 84 chems. (85%). The exercise highlighted areas of chem. where further development of the rulebase was required, either by extension of the scope of existing rules or by generation of new rules where a sound mechanistic rationale for the biol. activity could be established. Chems. likely to be acting as photoallergens were identified, and new rules for photoallergenicity have subsequently been written. At the end of the exercise, the refined rulebase was able to identify toxophores for skin sensitization for 82 of the 84 chems. in the BgVV list.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES
AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L189 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1976:505260 CAPLUS

DOCUMENT NUMBER: 85:105260

TITLE: Plant growth inhibitors of plant origin

AUTHOR(S): Schreiber, K.

CORPORATE SOURCE: Inst. Plant Biochem., Ger. Acad. Sci., Halle/Saale,
Ger. Dem. Rep.

SOURCE: Environmental Quality and Safety, Supplement (1975),
3(Pesticides), 483-5

CODEN: EQSSDX; ISSN: 0340-4714

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Of the 524 compds. of plant origin tested in the wheat seedling test,
71 (14%) were highly active and 126 significantly active as growth
retardants. Of the active compds., 58 (11%) were also active in the pea
bioassay. Only 5 of the tested compds. were shown to be antagonists of
gibberellin formation in *Fusarium moniliforme*. Twelve of the 28 naturally
occurring lactones (mostly sesquiterpenoid γ -lactones), 21 of 32
lichen constituents, and a relatively large no. of the steroids tested (28
of 90) were active.

L189 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1971:142092 CAPLUS

DOCUMENT NUMBER: 74:142092

TITLE: Correlation of structure and fragmentation modes of
costunolide and its derivatives

AUTHOR(S): Sathe, R. N.; Deshpande, Mrs. N. R.; Kulkarni, G. H.;
Kelkar, Govind R.; Das, K. Ganesh

CORPORATE SOURCE: Natl. Chem. Lab., Poona, India

SOURCE: Organic Mass Spectrometry (1971), 5(2), 197-202

CODEN: ORMSBG; ISSN 0030-493X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mass spectral studies of costunolide and its lactone derivs.,
revealed general fragmentation modes involving the losses of 44, 55, 57,
59, 71, 73, and 83 mass units from the mol. ion. The genesis of
these ions was established by high resolution, metastable transitions, and
D labeling studies. Comparisons were made with the mass spectra of the
C6-desoxy esters.

L189 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1963:482375 CAPLUS

DOCUMENT NUMBER: 59:82375

ORIGINAL REFERENCE NO. 59 15314h,15315a-h

TITLE Mexicanin. I A new sesquiterpene lactone related to
tenulin

AUTHOR(S): Dominguez, E.; Romo, J.

CORPORATE SOURCE: Univ. Nacl. Autonoma Mexico, Mexico City

SOURCE: Tetrahedron (1963), 19(9), 1415-21

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB cf. CA 55, 22365f. The mother liquors from isolation of helenalin from *Helenium mexicanum* evapd. and the residue crystd. from C₆H₆ gave 430 mg. product, m. 246-53.dblvert., recrystd. from CHCl₃-MeOH to yield mexicanin I (I, R = H) (II), m. 257-60.degree., [α]_D 42.5.degree. (CHCl₃). (All [α]_D were detd. at 20.degree. in CHCl₃.) II (150 mg.) in 4 ml. 1:1 Ac₂O-C₅H₅N heated 1 hr. on a steam bath and dild. with H₂O, filtered, and the ppt. crystd. from Me₂CO-Et₂O gave 130 mg. I (R = Ac) (III), m. 200-3.degree., [α]_D 26.5.degree.. II (150 mg.) in 20 ml. MeOH treated with CH₂N₂ (from 2 g. MeNHCONHNO) in Et₂O 30 min. at 20.degree. and the excess CH₂N₂ destroyed with a few drops of AcOH, the mixt. filtered off, and the residue washed with Et₂O gave 90 mg. II dipyrazoline, m. 185.degree. (decompn.). The nuclear magnetic resonance (n.m.r.) spectrum of III supported the assigned structure. II (200 mg.) in 8 ml. AcOH kept 1 hr. at 20.degree. with 150 mg. CrO₃ in 5 ml. 1:4 H₂O-AcOH, the H₂O-dild. soln. extd. with CHCl₃, the ext. washed with H₂O, 5% Na₂CO₃, and H₂O, evapd., and the residue recrystd. repeatedly from Me₂CO-Et₂O gave dehydroisomexicanin I (IV), m. 232-5.degree., [α]_D 129.degree.. II (300 mg.) in 150 ml. EtOAc hydrogenated over 80 mg. 10% Pd-C, the filtered soln. evapd., the oily residue crystd. from Et₂O, and the product crystd. from Me₂CO-C₆H₁₄ yielded di-hydroisomexicanin I (V), m. 144-6.degree., [α]_D 150-4.degree.. The cyclo-pentanone bond was reduced but the remaining bond at C-7-C-11 resisted hydrogenation. The salient features of the spectra of II, III, IV, and V, particularly the sharp signal due to a tertiary Me group, strikingly resemble those of parthenin, tenulin, and helenalin, which possess an abnormal guaianolide nucleus. V (170 mg.) in 6 ml. AcOH treated with 150 mg. CrO₃ in 5 ml. 1:4 H₂O-AcOH, the mixt. kept 80 min. at 20.degree., dild. with H₂O and extd. with CHCl₃, the ext. washed with H₂O, dried (Na₂SO₄), and evapd., the residue crystd. from Me₂CO-C₆H₁₄, and recrystd. from Me₂CO-Et₂O gave dehydrodihydroisomexicanin I (VI), m. 173-5.degree., [α]_D 184.degree.. VI (100 mg.) in 10 ml. AcOH refluxed 3 hrs. with 800 mg. powd. Zn, the filtered soln. dild. with H₂O and extd. with CHCl₃, the ext. washed with H₂O, 5% aq. NaOH, and H₂O, the dried ext. evapd., and the oily residue triturated with Et₂O gave 60 mg. needles recrystd. from Me₂CO-Et₂O to give dehydro-deacetyldihydroisotenulin (VII), m. 168-71.degree., [α]_D 20.degree.. IV (100 mg.) similarly reduced

gave 45 mg. VII, m. 147-9.degree., $[\alpha]_D^{22}$.degree. Differences in m.p. were apparently due to solvation. II (500 mg.) in 80 ml. C₆H₆ refluxed 6 hrs. with 2 ml. C₅H₁₁N and 2 ml. PhCH₂SH, the cooled mixt. washed with dil. HCl and H₂O, the dried soln. evapd., the residual oil (760 mg.) taken up in 70 ml. alc., the soln. refluxed 8 hrs. with 7 g. freshly prepd. Raney Ni with stirring, filtered, evapd., and the oily residue crystd. from Et₂O-C₆H₁₄ and recrystd. from Me₂CO-Et₂O gave deacetyldihydroisotenulin (VIII, R = H) (IX), m. 194-6.degree., $[\alpha]_D^{139}$.degree.. IX (60 mg.) in 2 ml. 1:1 Ac₂O-C₅H₅N heated 1 hr. on a steam bath, the soln. poured into H₂O, extd. with CHCl₃, the ext. washed with dil. HCl, H₂O, dil. aq. NaOH, and H₂O, dried, evapd., and the oily residue crystd. from Et₂O and recrystd. from Et₂O-C₆H₁₄ gave dihydroisotenulin VIII (R = Ac), m. 149-50.degree., $[\alpha]_D^{101}$.degree., 1770 cm.⁻¹ IX (40 mg.) in AcOH oxidized with CrO₃ and the isolated product crystd. from Me₂CO-C₆H₁₄ gave VII, m. 145-7.degree.. Accordingly, II is an "abnormal" guaianolide with asym. centers at C-1, C-5, C-8, and C-10 and lactone closure at C-8. The centers at C-6 and C-7 have the same configuration as in tetulin, but II differs from helenalin at C-6 and C-8 also, though both lactones have the same structural formula. II underwent a rearrangement in alk. medium to yield products of the "neo" type. II (140 mg.) in 20 ml. MeOH refluxed 3 min. with 140 mg. KOH in 2 ml. H₂O, the mixt. kept 30 min. at 20.degree., acidified with AcOH, concd., dild. with H₂O, extd. with CHCl₃, and the H₂O-washed ext. concd., treated with Et₂O, and filtered off gave 70 mg. platelets, recrystd. from CHCl₃-MeOH to give neomexicanin I (X, R = H) (XI) m. 259-63 degree., $[\alpha]_D^{10}$.degree.. The mother liquor from the 1st crystn. evapd., the oily residue crystd. from Me₂CO-C₆H₁₄, and the product recrystd. gave methoxydihydroneomexicanin I (XII), m. 168-70.degree., $[\alpha]_D^{27}$.degree.. Alk. treatment of II with KOH in tert-BuOH gave only XI. Acetylation of XI gave X (R = Ac), m. 170-2.degree. (Me₂CO-Et₂O), $[\alpha]_D^3$.degree.; n.m.r. spectrum showed similar signals to those reported for neohelenalin and neotenulin. III (500 mg.) in 60 ml. EtOAc hydrogenated over 60 mg. prerduced PtO₂ 4 hrs., the filtered soln. evapd., and the oily residue crystd. from Et₂O and recrystd. from Et₂O-C₆H₁₄ yielded 11-epidihydro-isotenulin, m. 109.degree., $[\alpha]_D^{48}$.degree.. Infrared, ultraviolet, and n.m.r. spectral data for most of the compds. were given.

L189 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1962:483404 CAPLUS

DOCUMENT NUMBER: 57:83404

ORIGINAL REFERENCE NO.: 57:16665d-i,16666a-h

TITLE: Terpenoids. XXXII. Absolute configuration of junenol and levojunenol and synthesis of junenol from costunolide

AUTHOR(S): Shaligram, A. M.; Rao, A. S.; Bhattacharyya, S. C.

CORPORATE SOURCE: Nat. Chem. Lab., Poona, India

SOURCE: Tetrahedron (1962), 18, 969-77

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. CA 54, 22709d; 57, 13808e. The hydrocarbon-rich fraction (b0 5 90-102.degree.) of distd. vetiver oil chromatographed on acid-washed Al₂O₃ (grades III and II) and the tail portion crystd. from petr. ether and sublimed gave levojunenol (I), m. 65.degree., [α]_D -57.degree. (I 1.18, all rotations in 95% alc.). I (298 mg.) heated (N atm.) 16 hrs. at 290.degree. with 446 mg. Se and the product taken up in petr. ether-C₆H₆, the concd. filtrate filtered through 30 g. Al₂O₃ (grade I) and eluted with petr. ether gave 228 mg. endalene, characterized as picrate, m. 95-6.degree., and s-trinitrobenzene deriv., m. 112.5-13.0.degree. I (1.024 g.) in 25 ml. AcOH hydrogenated 4 hrs. with 40 mg. prereduced PtO₂ and the product (970 mg.) sublimed gave dihydrolevojunenol (II), m. 115.degree., [α]_D +-.0 degree. (C 2.6). I (970 mg.) in 60 ml. dry EtOAc at -5.degree. ozonized 5 hrs. with evolution of HCHO and the mixt. evapd. at 40.degree. in vacuo, the ozonide decompd. by heating in 30 ml. H₂O on a steam bath 4 hrs. and the aq. layer extd. with Et₂O, washed with aq. NaHCO₃ and the neutral product isolated, the liquid residue (820 mg.) distd. at 135.degree. 0.1 mm and the solid product sublimed gave 740 mg. oxo alc. (III), C₁₄H₂₂O₂, m. 43.degree., [α]_D -11.5.degree. (c 2.00). The properties of I and its derivs. agree with those of an optical antipode of the dextrorotatory alc., junenol. III (420 mg.) in 4 ml. (HOCH₂CH₂)₂O heated (N atm.) 2 hrs. with 400 mg. KOH and 0.7 ml. 85% N₂H₄.H₂O at 110-15.degree. with occasional shaking and the H₂O evapd. at 195.degree., the mixt. refluxed 4 hrs. at 190.degree. and the cooled product dild. with 30 ml. H₂O, neutralized at 0.degree. with dil. HCl and extd. with Et₂O, the ext. neutralized and the dried soln. evapd., the product (383 mg.) dehydrogenated with 530 mg. Se at 280.degree. and the product chromatographed over 30 mg. Al₂O₃ (grade I) gave 2-Me₂CHC₁₀H₇, characterized as s-trinitrobenzene deriv., m. 107.degree.. Santanolide a (11.3 g., prepd. according to Kovacs, et al., CA 50, 11285f, from L-santonin) in 100 ml. Et₂O stirred at -10.degree. 1 hr. with addn. of 435 mg. LiAlH₄ in 100 ml. dry Et₂O and the mixt. stirred 2 hrs. before warming to 20.degree., the mixt. decompd. with H₂O and extd. with Et₂O gave 10.2 g. amorphous material showing a pos. Fehling test. The reduced product (3.17 g.) taken up in 14 ml. distd. (HOCH₂CH₂)₂O and shaken 30 min. at 20.degree. with 6 ml. 85% N₂H₄.H₂O, the soln. refluxed 2 hrs. (N atm.) with 3 g. KOH at 110-15.degree. and the H₂O evapd. at 195.degree., the soln. refluxed 3 hrs. at 190.degree. and the cooled product dild. with 50 ml. H₂O, repeatedly extd. with Et₂O and the residue on evapn. (700 mg.) chromatographed over 30 g. Al₂O₃ (grade III), eluted with 200 ml. 9:1 petr. ether-C₆H₆ and the fraction sublimed gave 388 mg. alc., C₁₅H₂₈O (IV), m. 53-4.degree.. As expected, the infrared spectrum of IV differed from that of II, and the same series of reactions was applied to

santanolide c (V). Costunolide (21.4 g., m. 106.degree.), [α .]D 128 degree. in 200 ml. AcOH contg. 10 ml. 65% HClO₄ hydrogenated with prereduced PtO₂ and the filtered soln. concd. to 70 ml., neutralized with Na₂CO₃ and extd. with Et₂O gave 6.3 g. V, m. 153-4.degree. (alc.), [α .]D 54.9 degree, also prepd. by hydrogenating a mixt. of costunolide and dehydrocostus lactone. V (9.9 g.) in 100 ml. Et₂O partially reduced with 500 mg. LiAlH₄ in 100 ml. Et₂O and totally reduced by Huang Minlon reduction gave material, purified by chromatography and sublimation to yield 379 mg. alc. (VI), m. 115.degree., [α .]D \pm 0.degree. (c 1.52), giving an infrared spectrum completely superimposable on that of II, and an identical n.m.r. spectrum, showing that VI and II are either identical or enantiomorphs. Mixed m.p. of VI and II gave a 20.degree. depression and the lack of identity was confirmed by measurement of rotatory dispersion curves. The mol. rotation difference ($\Delta M = -129$.degree.) between I and II is neg. but of the same magnitude as that between junenol (VII) and VI, which is of the same sign as that between eudesmol and dihydroeudesmol. Accordingly the abs. configuration of VII, I, and II can be depicted. I is the 1st naturally occurring eudesmanic compd. contg. both α -oriented C-10 Me and C-7 Me₂CH groups. The acid cyclization of dihydrocostunolide (VIII) gave a mixt. of 2 closely related lactones, the endocyclic unsatd. lactone (IX) and the exocyclic unsatd. isomeride (X), sep'd. by column chromatography. VIII (m. 77.degree., [α .]D 113.degree.) cyclized in AcOH and Ac₂O and the mixt. (62 g.) chromatographed on 2.4 kg. Al₂O₃ (grade III) and eluted successively with 10 l. petr. ether, 6 l. 1:1 petr. ether-C₆H₆, 6 l. C₆H₆, 6 l. alc., and 6 l. AcOH gave 27 g. fraction, m. 128 degree.; 0.8, 0.5, and 0.5 g. fraction, m. 60 degree.; and 24.5 g. fraction, m. 132.degree.. The 1st fraction repeatedly recrystd. from alc. and C₆H₁₄ and sublimed gave IX, m. 140.degree., [α .]D 85 degree. (c 1.402, CHCl₃), hydrogenated in AcOH with prereduced PtO₂ to give V. The last fraction recrystd. from C₅H₁₂ and sublimed gave the lactone X, m. 140.degree., [α .]D 140.degree. (c 3.5, CHCl₃), hydrogenated in AcOH with prereduced PtO₂ to give santanolide. X (1.1 g.) in 30 ml. dry EtOAc ozonized 5 hrs. at -5.degree. with evolution of HCHO, the product crystd. from alc. and sublimed at 150.degree./0.05 mm. gave 800 mg. oxo lactone (XI), m. 220.degree., [α .]D 71.48.degree. (c 1.525, CHCl₃). X (7.15 g.) in 150 ml. anhyd. Et₂O at -10.degree. stirred 1 hr. with addn. of 420 mg. LiAlH₄ in 100 ml. Et₂O and the mixt. stirred 2 hrs. at -10.degree. and 1 hr. at 20.degree., the washed and dried Et₂O layer evapd. in vacuo and the partially reduced lactone (6.8 g.) heated 5 min. on a steam bath in 40 ml. (HOCH₂CH₂)₂O and 11 ml. 85% N₂H₄.H₂O, the clear soln. kept 30 min. at 20 degree. and refluxed 2 hrs. at 110-15.degree. with 6 g. KOH, treated at 60.degree. with 20 ml. dry C₆H₆ and the C₆H₆ carefully evapd. at 130.degree. the procedure repeated 3 times and the H₂O-free soln. refluxed 2 hrs. at 150.degree., the cooled mass dild. with 50 ml. H₂O and extd.

with Et₂O, the product (800 mg.) chromatographed on 30 g. Al₂O₃ (grade III) and the column eluted with 200 ml. 9:1 petr. ether-C₆H₆, the fraction crystd. from petr. ether and sublimed gave VII, m. 61-2.degree., [α]_D 51.degree. (C 2.45). Ultraviolet, infrared, and nuclear magnetic resonance spectra were given.

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ACCESSION NUMBER: 1961:137670 CAPLUS

DOCUMENT NUMBER: 55:137670

ORIGINAL REFERENCE NO.: 55:26013g-i,26014a-i,26015a-i,26016a-d

TITLE: Cedrol stereochemistry and total synthesis

AUTHOR(S): Stork, Gilbert; Clarke, Frank H., Jr.

CORPORATE SOURCE: Columbia Univ.

SOURCE: J. Am. Chem. Soc. (1961), 83, 3114-25

CODEN: JACSAT; ISSN 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue

AB The total stereospecific synthesis of natural cedrol (I) was described.

Me₂C(CN)CH(CN)CO₂Et (II), b_{0.01} about 99-114.degree., b₄ 120-7.degree. (with decompn.), (250 g.) in 232 g. Me₃COH treated with 87 g. CH₂:CHCN and 5.0 cc. 40% choline in MeOH, the mixt. kept 6 hrs. at 0.degree., 18 hrs. at room temp., and 40 hrs. at 50.degree., cooled until crystals of Me₃COH appeared, the top layer evapd. on the steam bath in vacuo, the combined residue and bottom layer dild. with Et₂O, washed, evapd., the combined residues (638 g.) from 2 runs dissolved in 1300 cc. concd. HCl and 1300 cc. H₂O, the soln. refluxed 48 hrs., evapd. on the steam bath, cooled, filtered, evapd. to dryness, the residue treated with abs. EtOH, filtered, the filtrate (3500 cc.) refluxed 4.5 days with stirring with 700 cc. concd. H₂SO₄, 1 l. of EtOH distd., the residual soln. cooled, poured into satd. aq. NaCl, the oily layer worked up with Et₂O, and distd. gave 480 g. Me₂C(CO₂Et)CH(CO₂Et)(CH₂)₂CO₂Et (III), b_{0.01} about 154-6.degree., and 158 g. residue, which hydrolyzed and reesterified gave more III. III refluxed 3 hrs. in C₆H₆ with powd. Na yielded 64% di-Et 3,3-dimethylcyclopentan-2-one-1,4-dicarboxylate (IV), b. 132-3.degree. (in vacuo). PhCH₂OH (34.0 g.), 48 g. MeCHBrCO₂H, and about 0.5 g. p-MeC₆H₄SO₃H in 150 cc. C₆H₆ refluxed 18 hrs. with azeotropic removal of H₂O gave 55.5 g. MeCHBrCO₂CH₂Ph (V), b₇ 139-41.degree.. IV (50.0 g.) in 80 cc. dry C₆H₆ and 6.0 g. NaH in 100 cc. dry C₆H₆ refluxed until the H evolution ceased, decanted, the soln. distd. to remove 155 cc. C₆H₆, treated with the Na salt of 47.5 g. V in 100 cc. dry HCONMe₂, the mixt. heated at 50.degree. under N, kept 1 week, combined with the soln. of a 2nd run from 71.1 g. IV, and worked up yielded 179 g. 1-PhCH₂ ester (VI) of the HO₂CCHMe deriv. (VII) of IV, b. 175-92.degree. (in vacuo). VI (77.0 g.) in 150 cc. EtOAc hydrogenolyzed during 35 min. over 8.0 g. 10% Pd-C at an initial pressure of 50.0 lb. yielded 47.0 g. VII, prisms, m. 113-15.degree.

(cyclohexane). Na salt (11.6 g.) of VII in 100 cc. dry C₆H₆ contg 1.0 cc. C₅H₅N with 15 cc. (COCl)₂ added slowly to excess CH₂N₂ in Et₂O from 45 g. H₂NCON(NO)Me, the mixt. kept 1 hr. at 0 degree., evapd. on the steam bath, and the residual crude diazoketone treated in 150 cc. dry Et₂O with cooling with dry HCl gave 10.7 g. 1-ClCH₂COCHMe deriv. (VIII) of V, m. 72-3 degree. (cyclohexane). VIII (19.2 g.) and 20 g. powd. KI in 250 cc. AcOH treated slowly with stirring at 25 degree. with 100 g. Zn dust, stirred 6 hrs., dild. with 50 cc. H₂O, stirred overnight, filtered, the filtrate evapd., the residue partitioned between H₂O and Et₂O, and the Et₂O soln. worked up gave 17.1 g. 1-AcMeCH deriv. (IX) of V, m. 55-60 degree. (petr. ether), semicarbazone m. 191-3 degree. (aq. EtOH). Crude IX (4.3 g.) in 30 cc. dry Me₃COH and 0.7 g. K in 70 cc. dry Me₃COH refluxed 3 hrs. under N, dild. with H₂O, and extd. with Et₂O gave 1.47 g. mobile oil; a 0.4-g. portion, 0.45 g. semicarbazide, 1.65 cc. C₅H₅N, and 8 cc. EtOH refluxed 1.5 hrs. and kept overnight yielded the semicarbazone of X, m. 174-6 degree. (EtOAc-cyclohexane). IX (20.1 g.) and 3.0 g. K in 300 cc. dry Me₃COH kept 10 min. at room temp. gave 18.6 g. crude aldol, which, refluxed 1 hr. with 2.0 g. p-MeC₆H₄SO₃H.H₂O in 400 cc. C₆H₆, yielded 15.2 g. XI, m. 46-56 degree. (petr. ether), 23.6 g. crude XI recrystd. twice from petr. ether gave 10.8 g. of 1 isomer, m. 65-7 degree., of XI. XI (504 mg.), m. 65-7 degree., in 16 cc. abs. EtOH hydrogenated 20 min. at 25.4 degree. over 136 mg. 10% Pd-C yielded 325 mg. XII, m. 33.5-35.0 degree. (petr. ether); 2,4-dinitrophenylhydrazone (XIII) m. 160-1 degree.; recrystd. from EtOAc-EtOH, it gave needles, which slowly changed to prisms on standing in the soln. XI (307 mg.) in 2 cc. dry tetrahydrofuran and 15 cc. dry liquid NH₃ treated with stirring with 15-20 mg. Li and then with 0.6 g. NH₄Cl, the NH₃ evapd., and the residual yellowish oily XII (271 mg.) chromatographed from petr. ether on Al₂O₃ yielded oily colorless XII; XIII m. 152-4 degree. (EtOAc-EtOH). XII (655 mg.) in 10 cc. 80% EtOH refluxed 36 hrs. under N with 2.0 g. KOH, poured into H₂O, washed with Et₂O, acidified with concd. HCl, extd. with Et₂O, the gummy residue (528 mg.) from the ext. refluxed 3 hrs. with 6 cc. Ac₂O, evapd. under a stream of N, and the dark residue sublimed in vacuo at 160-70 degree. gave 174 mg. anhydride (XIV), prisms, m. 171-3 degree. (Et₂O). The XIV refluxed 20 hrs. with 6 cc. 50% aq. dioxane and the oily product treated with MeCHN₂ from 5 cc. EtO₂CN(NO)Et yielded 102 mg. XII; XIII m. 159-61 degree.. XII (1.03 g.) in 10 cc. CHCl₃ and 1.0 cc. (CH₂SH)₂ satd. with dry HCl and kept at 0 degree. overnight yielded 0.86 g. XV, m. 75-6 degree. (pentane). XV (1.32 g.) in 125 cc. abs. EtOH stirred 15 hrs. at reflux with 50 g. Raney Ni alloy gave 0.86 g. di-Et ester (XVI) of dl-norcedrenedicarboxylic acid (XVII), mobile oil. XVII (0.82 g.) and 2.0 g. KOH in 10 cc. 95% EtOH refluxed 24 hrs., poured into H₂O, and acidified with 10 cc. concd. HCl gave 0.62 g. XVII, m. 221-3 degree. (Et₂O-pentane). XVII (300 mg.) in Me₂CO with 410 mg. quinine in acetone yielded 252 mg. quinine salt (XVIII) of (-)-XVII, m. 209-10 degree. (CHCl₃Me₂CO), [α]_D²⁵ -122 degree. (c 1.00, CHCl₃).

XVII (121 mg.) shaken 15 min. with 5 cc. 6N HCl gave 46 mg (-)-XVII, m. 212-13.degree., [alpha]_D²⁵ -38.9 +/- 1.5.degree. (c 1.08, Me₂CO); natural (-)-XVII m. 213-14.degree., [alpha]_D²⁵ -38.3 +/- 1.0.degree. (c 1.09, Me₂CO). (-)-XVII (10.00 g.) with excess CH₂N₂ in Et₂O yielded 10.59 g XIX (R = CO₂H) (XX), b_p 95-132 degree. XX (10.5 g.) and 2.4 g. KOH in 35 cc. abs. EtOH refluxed 2 hrs. gave about 2 g. unchanged XX and 6.20 g. XIX (R = CO₂Me) (XXI), m. 129-32 degree. XXI (8.05 g.) and 20 cc. (COCl)₂ kept 1.5 hrs. at room temp., dild., evapd. with C₆H₆, the residual XIX (R = COCl) treated 1 hr. with CH₂N₂ from 45 g. H₂NCON(NO)Me in Et₂O, the resulting crude XIX (R = CON₂) in 50 cc. dry Et₂O satd. with dry HCl, evapd. in vacuo on the steam bath, the XIX (R = COCH₂Cl) treated with cooling and stirring with 9 g. KI in 100 cc. 80% AcOH and 45 g. powd. Zn, and the mixt. stirred at room temp. overnight yielded 7.73 g. crude XIX (R = Ac) (XXII); 2,4-dinitrophenylhydrazone m. 140-2 degree. (cyclohexane). XXII (7.73 g.) and 3.0 g. KOH in 120 cc. dry Me₃COH refluxed 3 hrs. yielded 4.90 g. XXIII, m. 202-4.degree. (dioxane) XXIII (2.00 g.) refluxed 17 hrs. with stirring with 2.00 g. LiAlH₄ in 50 cc. dry Et₂O gave 1.91 g. (crude) XXIV, m. 120-1.degree. (cyclohexane). Crude XXIV oxidized with CrO₃-C₅H₅N and the crude product chromatographed on Al₂O₃ yielded XXV; 2,4-dinitrophenylhydrazone m. 146-7.degree. XXIII (2.84 g.) in 50 cc. abs. EtOH contg. 0.10 g. p-MeC₆H₄SO₃H H₂O distd. during 4 hrs. to remove 53 cc. distillate gave 2.82 g. oily mixt. of the enol ethers, the crude mixt. in 25 cc. dry Et₂O reduced with 1.0 g. LiAlH₄ in 150 cc. Et₂O and the crude product (2.45 g.) refluxed 1.5 hrs. with 0.20 g. p-MeC₆H₄SO₃H H₂O in 50 cc. C₆H₆ yielded 508 mg. XXIV. XXIII (5.21 g.) in dry Et₂O reduced with 7.77 g. LiAlH₄ in 250 cc. dry Et₂O, the crude foamy product (4.11 g.) treated 17 hrs. at room temp. with 8.43 g. CrO₃ in 84 cc. C₅H₅N, the mixt. poured into 750 cc. Et₂O, filtered, and the filtrate worked up gave 2.81 g. pale yellow oily aldehyde-ketone; a 2.50-g. portion refluxed 1.45 hrs. with 12.5 g. KOH in 500 cc. H₂O at about 50.degree. and 90 mm., extd. with Et₂O, and the crude oily product (2.02 g.) chromatographed on Al₂O₃ yielded 1.47 g. XXVI; 2,4-dinitrophenylhydrazone, brilliant red prisms, m. 164-7.degree. (MeOH) XXVI (527 mg.) in 10 cc. abs. EtOH hydrogenated 1 hr. at 23.degree. gave 524 mg. oily XXV; 2,4-dinitrophenylhydrazone, yellow needles changing to prisms on standing in soln., m. 146-7 degree. (MeOH). XXIV (219 mg.) in 2.2 cc. C₅H₅N treated 23 hrs. at room temp. with 224 mg. CrO₃ in 2.2 cc. C₅H₅N yielded 190 mg. XXV. XXV (164 mg.) reduced during 17 hrs. with 0.40 g. LiAlH₄ in 30 cc. Et₂O gave 140 mg. XXIV. XXV (446 mg.) in dry Et₂O added slowly to MeLi from 1.8 g. Li and 6 cc. MeI in 40 cc. dry Et₂O and the mixt. refluxed 18.5 hrs. with stirring gave 1, collected in 4 fractions: 380 mg., m. 80-1.degree.; 340 mg., m. 83-7 degree.; 284 mg., m. 85-7.degree.; 215 mg., m. 86-7.degree., needles, [alpha]_D²⁵ 10.5 +/- 0.8.degree. (c 5.00); natural I m. 86-7.degree., [alpha]_D²⁵ 9.9 +/- 0.4.degree. (c 5.00, CHCl₃).

L189 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER 1962:38646 CAPLUS

DOCUMENT NUMBER: 56:38646

ORIGINAL REFERENCE NO.: 56:7368c-i

TITLE: CXXXI. Isolation and structure of costunolide
, balchanolide, isobalchanolide, and
hydroxybalchanolide, sesquiterpenic lactones of
germacrane type from *Artemisia balchanorum*

AUTHOR(S): Krasch, H.; Herout, V.; Suchy, M.; Sorm, F.

CORPORATE SOURCE: Ceskoslov. Akad. Ved., Prague

SOURCE: Collection Czechoslov. Chem. Commun. (1961), 26,
2612-23

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB Costunolide (I), m. 106.degree. (MeOH), [α]_D²⁰ 128.degree. (c 10.5, CHCl₃), isobalchanolide (II), m. 133.degree. (iso-Pr₂O-Me₂CO), [α]_D²⁰ 122.degree. (c 2.08, CHCl₃), balchanolide (III), m. 154.degree. (iso-Pr₂O-Me₂CO), [α]_D²⁰ 183.degree. (c 1.84, CHCl₃), and hydroxybalchanolide (IV), m. 163.degree. [α]_D²⁰ 105.degree. (c 2.71, EtOH). Hydrogenation of I in MeOH over 5% Pd on C gave dihydrocostulolide (V), m. 79-80.degree. (MeOH). Hydrogenation of I in AcOH over PtO₂ gave oily hexahydrocostunolide. If 2 drops of 70% HClO₄ were added to the mixt., the H uptake amounted to 2.0 double bonds and santanolide C (VI) was the chief product, m. 155.degree. (EtOH), [α]_D²⁰ 50.1.degree. (c 4.0, CHCl₃), along with 2 compds., m. 114.degree. (MeOH) and m. 79 degree., isolated by chromatography. Refluxing V with AcOH and Ac₂O, evapg. the mixt., and crystg. from MeOH gave a compd., m. 122.degree., whose recrystn. from 1:5 C₆H₆-petr. ether gave 3-santenolide (VII), m. 135.5.degree.. Hydrogenation of VII in AcOH over PtO₂ (H uptake amounted to 1.05 double bonds) followed by crystn. and chromatography gave VI along with santanolide A, m. 153.degree. (80% aq. EtOH). The location of the double bonds in I (CA 54, 3489b) was verified by ozonization of V in AcOH and decompn. of the ozonides in boiling HNO₃: the chief product, a lactonedicarboxylic acid, R_f 0.38 (BuOAc-2% HCO₂H), was identical with that prepd. earlier from artabsin. Acetylisobalchanolide, m. 139-40.degree., [α]_D²⁰ 18.5.degree. (c 1.8, CHCl₃), was hydrogenated in MeOH over PrO₂ to give tetrahydroacetylisobalchanolide (VHI), m. 125.degree. (iso-Pr₂O), identical with tetrahydroacetylbalchanolide, prepd. earlier. Hydrolysis of VIII with K₂CO₃ in MeOH followed by oxidn. of the oily product with CrO₃ in AcOH gave an oxo lactone, C₁₅H₂₄O₃, m. 136.5.degree. (iso-Pr₂O), identical with that prepd. earlier from arctiopicrin and cnicin. Oxidn. of II-IV with satd. aq. KMnO₄ gave a mixt. of (CH₂CO₂H)₂ and MeCOCH₂CH₂CO₂H, identified by paper chromatography. Oxidn. of III with CrO₃ in C₅H₅N gave an oxo lactone, C₁₅H₂₀O₃, m. 110 degree. (iso-PrO₂).

Hydrogenation of IV in AcOH over PtO₂ gave tetrahydrohydroxybalchanolide C₁₅H₂₆O₄, m. 101.degree. (iso-Pr₂O-Me₂CO), whose oxidn. with CrO₃ in AcOH gave a hydroxy oxo lactone, C₁₅H₂₄O₄ (IX), m. 127.degree. (isoPr₂O-Me₂CO). Structures of II-IV and some of their derivs. were suggested. II and III differ in the location of the double bonds, or, in their steric arrangement (cis-trans-isomerism) only.

L189 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1962:423334 CAPLUS

DOCUMENT NUMBER: 57:23334

ORIGINAL REFERENCE NO. 57:4699b-g

TITLE: Conversion of costunolide to junenol

AUTHOR(S): Shaligram, A. M.; Rao, A. S.; Bhattacharyya, S. C.

CORPORATE SOURCE Natl Chem. Labs., Poona, India

SOURCE: Chem. Ind. (London) (1961) 671

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB (All [α]D in EtOH.) Previously (CA 54, 22709d) the abs.

configuration was established of the enantiomeric sesquiterpene alcs. junenol (I) and levojunenol (II), on the basis of conversion of santanolide c (III) to dihydrojunenol (IV). The structure and conversion of the lactone V to dextrorotatory I was now described. Cyclization of VI gave a product (VIa), m. 117.degree., much lower than that of the lactone (VII), previously (CA 54, 3489d) obtained by cyclization of VI. Chromatography of VIa gave VII, m. 140.degree., [α]D 85.degree. (c 1.402), giving III on catalytic hydrogenation, giving no CH₂O on ozonolysis, this structure also being in agreement with its infrared (ν 790 and 1794 cm.⁻¹) and ultraviolet spectra (ϵ 210 287, ϵ 215 1435, ϵ 220 385), and an isomer (V), m. 140.degree., [α]D 140.degree. (c 3.55), this structure being assigned on the basis of infrared (ν 885, 1633, and 1764 cm.⁻¹) and ultraviolet spectra (ϵ 210 377, ϵ 215 120, ϵ 220 75), giving santanolide a on catalytic hydrogenation, giving on ozonolysis CH₂O (dimedon deriv. m. 189.degree.) and the oxo lactone (VIII), m. 210.degree., [α]D 71.degree. (c 1.525). V was converted to d-I as described previously for the conversion of III to IV. d-I m. 61-2.degree., [α]D 51.degree. (c 2.45), its infrared spectrum being identical with that of II.

L189 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1950:711 CAPLUS

DOCUMENT NUMBER: 44:711

ORIGINAL REFERENCE NO.: 44:138f-i, 139a-b

TITLE: Helenalin. I. Isolation and properties

AUTHOR(S) Adams, Roger; Herz, Werner

SOURCE: J. Am. Chem. Soc. (1949), 71, 2546-51

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE Journal

LANGUAGE: Unavailable

AB cf. Clark, C.A. 30, 8236.2. Helenalin (I), $C_{15}H_{18}O_4$, was isolated from *Helenium microcephalum* by the method of C. in av. yields of 0.38% and, crystd. 3 times from abs. EtOH, m. 176-8.degree.; the residue, crystd. 3 times from abs. EtOH, m. 165.5-6.degree., $[\alpha]_D^{25} -102.8$ degree. (0.0728 g. in 2 ml. 95% EtOH), the infrared spectrum is identical with that of C.'s prepn. The Ac deriv. (II), m. 179.5-80.5.degree., absorption max. at 221 and 316 m. μ . (ϵ 12,600 and 61). o-Bromobenzoyl deriv. of I, m. 162-3.degree.; p-nitro-benzoyl deriv. of I, with 0.5 mol. C_6H_6 , m. 111.degree.; 3,5-dinitrobenzoyl deriv., with 0.5 mol. C_6H_6 , m. 213.degree.. Tetra-hydrohelenalin (III), m. 175-6.degree., infrared spectrum given; Ac deriv. (IV), m. 145.degree. (prepd. by acetylation of III or by reduction of II in AcOEt over Pt oxide); the spectra of III and IV are similar [absorption max. at 287 m. μ . (ϵ 36)]. IV (115 mg.) and 64 mg. piperonal in 2 ml. abs. EtOH, treated with 5 ml. satd. EtOH-HCl and kept 18 hrs., give the piperonylidene deriv. of II, $C_{25}H_{25}O_7Cl$, pale yellow, m. 214.degree.. I (50 mg.) in 1 ml. AcOH, treated with 1.03 g. Br in 15 ml. AcOH at room temp., gives 71 mg. dibromohelenalin (V), decomp. 130.degree.; recrystn. of V from 50% EtOH or 50% AcOH gives bromohelenalin, m. 164.5.degree., absorption max. at 248 and 314 m. μ . (ϵ 6300 and 97); reduction over Pt oxide gives III. II and Br in Ac-OH, irradiated with an elec. light, give a di-Br deriv., decomp. 153-4.degree.; boiled 0.5 hr. with 50% EtOH, it gives the Br deriv., m. 153.5.degree.. I and $NH_2OH \cdot HCl$ in abs. EtOH contg. AcONa, refluxed 16 hrs., give the compd. $C_{15}H_{22}N_2O_5$, amorphous, m. 200-3.degree. (decompn.). I (1 g.) and 4 g. (iso-PrO) $_3$ Al in 20 ml. iso-PrOH, refluxed 5 hrs., the solvent removed by slow distn., 20 ml. iso-PrOH added, the distn. continued until the test for Me_2CO is neg., the product decompd. with 25 ml. 10% H_2SO_4 , and extd. with ether, give 100 mg. of the compd., $C_{15}H_{20}O_4$, b.p. 200-30.degree. (bath temp.); it did not yield a solid ester; in 1 expt. there resulted 29 mg. of a compd., m. 196-201.degree., which may be an intramol. oxidation-reduction product. I and O_3 give 50-60% HCHO; II gives 45% HCHO. Chem. and phys. evidence establishes the presence of the grouping $RCOCH \cdot CR_2$, possibly a part of a 5-membered ring, and makes likely the presence of a lactone ring. These functional groups account satisfactorily for all 4 O atoms and for 1 of the double bonds. The other double bond is unconjugated and part of a terminal CH_2 group.

LG ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
 ACCESSION NUMBER: 2002:107101 CAPLUS
 DOCUMENT NUMBER: 136:161354
 TITLE: Terpene compound compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2, and use as antiinflammatory agents
 INVENTOR(S): Babish, John G.; Howell, Terrence M.; Pacioretty, Linda M.
 PATENT ASSIGNEE(S): Ashni Naturaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 67 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009698	A1	20020207	WO 2001-US24053	20010801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RC, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SI, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, ME, NE, SN, TD, TG				
US 2002077350	A1	20020620	US 2001-919510	20010731
PRIORITY APPLN. INFO.:			US 2000-221190P	P 20000801
			US 2001-919510	A 20010731

AS A formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component, a **diterpene triepoxide lactone** species or a **sesquiterpene lactone** species and, as a second component, at least one member selected from the group consisting of a **diterpene triepoxide lactone** species, a **sesquiterpene lactone** species, a diterpene **lactone** species, and a triterpene species or derivs. thereof, with the proviso that the same first component cannot also serve as the second component, and provides synergistic antiinflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LG ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
 ACCESSION NUMBER: 2002:466702 CAPLUS
 DOCUMENT NUMBER: 137:41737
 TITLE: Combinations of **sesquiterpene lactones** and **diterpene triepoxide lactones** for synergistic inhibition of cyclooxygenase-2
 INVENTOR(S): Babish, John G.; Howell, Terrence; Pacioretty, Linda
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 18 pp.
 CODEN: USXXCC
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002077299	A1	20020620	US 2001-919349	20010731
US 2002076452	A1	20020620	US 2001-919506	20010731

PRIORITY APPLN. INFO.: US 2000-222167P P 20000801

AB A novel formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component an effective amt. of **diterpene triepoxide lactone** species and an effective amt. of a second component of **sesquiterpene lactone** species or derivs. thereof, and provides synergistic anti-inflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol. For example, a lotion designed to contain 0.1 % triptolide and 0.1% parthenolide was applied to affected areas of patients with acne rosacea and results showed improvement as compared with the placebo control.

L6 ANSWER 3 OF 3 IFIPAT COPYRIGHT 2003 IFI DUPLICATE 3
 AN 10133723 IFIPAT;IFIUDB;IFICDB
 TITLE: COMPOSITIONS EXHIBITING SYNERGISTIC INHIBITION OF THE EXPRESSION AND/OR ACTIVITY OF CYCLOOXYGENASE-2; FOR THERAPY OF INFLAMMATION
 INVENTOR(S): Babish; John G., Brooktondale, NY, US
 Howell; Terrence, Dryden, NY, US
 Pacioretty; Linda, Brooktondale, NY, US
 PATENT ASSIGNEE(S): Ashni Naturaceuticals, Inc.
 AGENT: THORPE NORTH WESTERN, 8180 SOUTH 700 EAST, SUITE 200, P.O. BOX 1219, SANDY, UT, 84070, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2002077350	A1	20020620
APPLICATION INFORMATION:	US 2001-919510		20010731

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 2000-222190P	20000801 (Provisional)
FAMILY INFORMATION:	US 2002077350	20020620
DOCUMENT TYPE:	Utility Patent Application - First Publication	
FILE SEGMENT:	CHEMICAL APPLICATION	
NUMBER OF CLAIMS:	38 6 Figure(s).	

DESCRIPTION OF FIGURES:

FIG. 1 illustrates the general chemical structure of (A1) the diterpene triepoxide **lactone** genus and (A2) triptolide as a species within that genus.
 FIG. 2, (A1) and (A2) respectively, illustrate the general chemical structures of the **sesquiterpene lactone** genus and parthenolide as a species within that genus.
 FIG. 2 (B1) and (B2) respectively illustrate the general chemical structures of the diterpene **lactone** genus and andrographolide as a species within that genus.
 FIG. 2 (C1), (C2) and (C3) respectively, illustrate the general chemical structures of the triterpene genus and ursolic acid and oleanolic acid as species within that genus.
 FIG. 3 provides a schematic for the experimental design of EXAMPLE 1.
 FIG. 4(a)-(q) are line graphs depicting the percent inhibition of COX-2 enzyme protein expression by individual and the combinations of the tested materials, as described in EXAMPLE 17, in the absence and presence of arachidonic acid

(AA).

AB A novel formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component, a **diterpene triepoxide lactone** species or a **sesquiterpene lactone** species and, as a second component, at least one member selected from the group consisting of a **diterpene triepoxide lactone** species, a **sesquiterpene lactone** species, a **diterpene lactone** species, and a **triterpene** species or derivatives thereof with the proviso that the same first component cannot also serve as the second component., and provides synergistic anti-inflammatory effects in response to physical or chemical injury or abnormal immune stimulation due to a biological agent or unknown etiology.

CLMN 38 5 Figure(s).

FIG. 1 illustrates the general chemical structure of (A1) the diterpene triepoxide **lactone** genus and (A2) triptolide as a species within that genus.

FIG. 2, (A1) and (A2) respectively, illustrate the general chemical structures of the **sesquiterpene lactone** genus and parthenolide as a species within that genus.

FIG. 2 (B1) and (B2) respectively illustrate the general chemical structures of the diterpene **lactone** genus and andrographolide as a species within that genus.

FIG. 2 (C1), (C2) and (C3) respectively, illustrate the general chemical structures of the triterpene genus and ursolic acid and oleanolic acid as species within that genus.

FIG. 3 provides a schematic for the experimental design of EXAMPLE 1.

FIG. 4(a)-(g) are line graphs depicting the percent inhibition of COX-2 enzyme protein expression by individual and the combinations of the tested materials, as described in EXAMPLE 17, in the absence and presence of arachidonic acid (AA).